AMENDMENTS TO THE CLAIMS

1.   (**Original**) A method of modulating a biological response in a cell, the method comprising contacting the cell with at least one agent that modulates the expression or activity of Errα or Gabp, wherein the biological response is

> (a) expression of at least one OXPHOS gene;
>
> (b) mitochondrial biogenesis;
>
> (c) expression of Nuclear Respiratory Factor 1 (NRF-1);
>
> (d) β-oxidation of fatty acids;
>
> (e) total mitochondrial respiration;
>
> (f) uncoupled respiration;
>
> (g) mitochondrial DNA replication;
>
> (h) expression of mitochondrial enzymes; or
>
> (i) skeletal muscle fiber-type switching.

2-16. (**Canceled**)

17.   (**Withdrawn - Currently Amended**) A method of determining whether ~~if~~ an agent is a potential agent for the treatment of a disorder that is characterized by glucose intolerance, insulin resistance or reduced mitochondrial function, the method comprising determining whether ~~if~~ the agent increases:

> (i) the expression or activity of Errα or Gabp in a cell; or
>
> (ii) the formation of a complex between a PGC-1 polypeptide and (i) an Errα polypeptide; or (ii) a Gabp polypeptide;

wherein an agent that increases (i) or (ii) is a potential target for the treatment of the disorder.

18.   (**Canceled**)

19. (**Withdrawn**) The method of claim 17, wherein the agent increases the formation of the complex, and wherein the agent increases the biological response.

20. (**Withdrawn**) The method of claim 19, wherein the agent decreases the formation of the complex, and wherein the agent decreases the biological response.

21-34. (**Canceled**)

35. (**Original**) A method of reducing the metabolic rate of a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of an agent which decreases the expression or activity of at least one of the following:

(i) Errα;

(ii) Gabpa;

(iii) a gene having an Errα binding site, a Gabpa binding site, or both; or

(iv) a transcriptional activator which binds to an Errα binding site or to a Gabpa binding site;

thereby reducing the metabolic rate of the patient.

36-41. (**Canceled**)

42. (**Withdrawn - Currently Amended**) A method of identifying a susceptibility locus for a disorder that is characterized by reduced mitochondrial function, glucose intolerance, or insulin intolerance in a subject, the method comprising

(i) identifying at least one polymorphism ~~polymorphisms~~ in a gene, or linked to a gene, wherein the gene (a) has an Errα binding site, a Gabpa binding site, or both; or (b) is Errα, Gabpa, or Gabpb;

(ii) determining whether ~~if~~ at least one polymorphism is associated with the incidence of the disorder,

wherein if a polymorphism is associated with the incidence of the disorder then the gene having the polymorphism, or the gene to which the polymorphism is linked, is a susceptibility locus.

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43-46. **(Canceled)**

47.   **(Withdrawn -Currently Amended)** A method of determining whether if a subject is at risk of developing a disorder which is characterized by reduced mitochondrial function, the method comprising determining whether if a gene from the subject contains a mutation which reduces the function of the gene, wherein the gene has an Errα binding site, a Gapba binding site, or both, wherein if a gene from the subject contains the mutation then the subject is at risk of developing the disorder.

48-77. **(Canceled)**

78.   **(Withdrawn -Currently Amended)** A method of detecting statistically-significant differences in the expression level of at least one biomarker belonging to a biomarker set, between the members of a first and of a second experimental group, comprising:

(a) obtaining a biomarker sample from members of the first and the second experimental groups;

(b) determining, for each biomarker sample, the expression levels of at least one biomarker belonging to the biomarker set and of at least one biomarker not belonging to the set;

(c) generating a rank order of each biomarker according to a difference metric of its expression level in the first experimental group compared to the second experimental group;

(d) calculating an experimental enrichment score for the biomarker set by applying a non-parametric non-parametric statistic; and

(e) comparing the experimental enrichment score with a distribution of randomized enrichment scores to calculate the fraction of randomized enrichment scores greater than the experimental enrichment score, wherein a low fraction indicates a statistically-significant difference in the expression level of the biomarker set between the members of the first and of the second experimental group.

79-92. **(Canceled)**

93. **(Currently Amended)** A method of identifying an agent that regulates expression of OXPHOS-CR genes, the method comprising

    (a) contacting (i) an agent to be assessed for its ability to regulate expression of OXPHOS-CR genes with (ii) a test cell; and

    (b) determining whether the expression of at least two OXPHOS-CR gene products show a coordinate increase~~change~~ in the test cell compared to an appropriate control, wherein a coordinate increase~~change~~ in the expression of the OXPHOS-CR gene products indicates that the agent regulates the expression of OXPHOS-CR genes.

94-105. **(Canceled)**

106. **(Currently Amended)** The method of claim 93, wherein a coordinate increase~~change~~ in the expression of the OXPHOS-CR gene products further indicates that the agent is a potential enhancer~~modulator~~ of the expression or activity of Errα or Gabp.

107. **(Currently Amended)** The method of claim 106, wherein a coordinate increase ~~change~~in the expression of the OXPHOS-CR gene products further indicates that the agent is a potential agent for enhancing ~~modulating~~ mitochondrial biogenesis, expression of Nuclear Respiratory Factor 1 (NRF-1), β-oxidation of fatty acids, total mitochondrial respiration, uncoupled respiration, mitochondrial DNA replication, expression of mitochondrial enzymes, or skeletal muscle fiber-type switching.

108. **(Currently Amended)** The method of claim 93, wherein the agent to be assessed is a small molecule~~method comprises determining whether the expression of at least two OXPHOS-CR gene products show a coordinate increase in the test cell as compared to an appropriate control~~.

109.   **(Currently Amended)** The method of claim <u>93</u> ~~108~~, wherein a coordinate increase in the expression of the OXPHOS-CR gene products indicates that the agent is a potential agent for the treatment of a disorder that is characterized by glucose intolerance, insulin resistance or reduced mitochondrial function.

110.   **(Currently Amended)** The method of claim <u>93</u> ~~108~~, wherein a coordinate increase in the expression of the OXPHOS-CR gene products further indicates that the agent is a potential agent for increasing expression or activity of Errα or Gabp.

111.   **(Previously Presented)** The method of claim 110, wherein an agent that increases expression or activity of Errα or Gabp is a potential agent for the treatment of a disorder that is characterized by glucose intolerance, insulin resistance or reduced mitochondrial function.

112.   **(Currently Amended)** The method of claim 110, wherein <u>the test cell is a mammalian cell</u> ~~a coordinate increase in the expression of the OXPHOS-CR gene products indicates that the agent is a potential agent for increasing mitochondrial biogenesis, expression of Nuclear Respiratory Factor-1 (NRF-1), β-oxidation of fatty acids, total mitochondrial respiration, uncoupled respiration, mitochondrial DNA replication, expression of mitochondrial enzymes, or skeletal muscle fiber-type switching~~.

113.   **(Withdrawn)** The method of claim 93, further comprising assessing the effect of the agent on mitochondrial number or on a mitochondrial function.

114.   **(Withdrawn)** The method of claim 93, further comprising assessing whether the agent increases a desired biological response that is impaired in subjects having a disorder that is characterized by glucose intolerance, insulin resistance, or decreased mitochondrial function.

115.   **(Withdrawn - Currently Amended)** The method of claim 93, <u>wherein step (a) is performed in vitro, and the method</u> further <u>comprises</u> ~~comprising~~ administering the agent to a mammalian organism.

116.   (**Withdrawn**) The method of claim 115, wherein the mammalian organism is human.

117.   (**Withdrawn**) The method of claim 115, wherein the mammalian organism is a test animal that serves as a model for a disorder characterized by glucose intolerance, insulin resistance, or decreased mitochondrial function.

118.   (**New**) The method of claim 93, wherein the test cell is a mammalian cell.

119.   (**New**) The method of claim 118, wherein the test cell is a skeletal muscle cell.

120.   (**New**) The method of claim 118, wherein the test cell is in an organism.

121.   (**New**) The method of claim 118, wherein the agent to be assessed is a small molecule.

122.   (**New**) The method of claim 93, wherein the method is performed in parallel on multiple populations of cells and each population is contacted with a different agent to be assessed.

123.   (**New**) The method of claim 122, wherein the agents are members of a compound library.

124.   (**New**) The method of claim 109, wherein the agent is useful for treating a human suffering from a disorder that is characterized by glucose intolerance, insulin resistance or reduced mitochondrial function.

125.   (**New**) The method of claim 111, wherein the agent is useful for treating a human suffering from a disorder that is characterized by glucose intolerance, insulin resistance or reduced mitochondrial function.

126.   (**New**) The method of claim 93, further comprising determining whether the agent also regulates expression of genes that are not OXPHOS-CR genes.